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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/751,654	12/29/2000	Sergei G. Bavykin	0003/00797	8872

7590 01/28/2004

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/751,654	BAVYKIN ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to the office action filed on October 1, 2003 has been entered and considered. Claims 1-26 are pending.

2. This application has a filing date as December 29, 2000 and claims no priority date.

Response to arguments

3. Applicants' response to the office action is fully considered and found persuasive in part.

4. With reference to the rejection under obviousness double-patenting, Applicants arguments are fully considered and the rejection is with drawn herein in view of the Terminal Disclaimer.

5. The following is the rejection made in the previous office action under 35 USC 103(a):

Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Proudnikov et al. (Nucleic Acids Res., Vol. 24, No. 22, pp. 4535-4532, 1996) in view of Ekenberg (USPN. 6,218,531).

Proudnikov et al. teach a method for labeling genetic material wherein Proudnikov et al. teach (b, and c) loading the genetic material in a column and fragmenting and labeling of the genetic material in the column via creating radical-mediated process at the same time (see page 4536, column 2, paragraphs 4-5, page 4537, column 1, paragraph 1 and 4538, column 1, and paragraphs 1-6); and (d) eluting the labeled genetic material from the column (see page 4537, column 1, paragraph 1, page 4540, column 2, paragraph 2-3). Proudnikov et al. also teach (i) contacting double-stranded nucleic acid with radical-generating complexes to produce aldehyde moieties (see page 4538, column 1, paragraph 2); (ii) reacting the aldehyde moieties with amine to produce condensation product and contacting the codensation product with a chromophore (see 4538, column 1, paragraph 2, page 4539, column 2, paragraph 2, page 4540, column 1,

paragraph 1) (iii) column comprises a syringe for subjecting the column to pressure (see page 4537, column 1, paragraph 1) the labeling of genetic material was carried at temperatures ranging from 20^0 - 37^0 C (see page 4536, column 2, paragraph 3-5, page 4537, column 1, paragraph 2) and the labeling is done in anaerobic (in the column) or aerobic conditions (out side the column or in solution) (see page 4536, column 2, paragraph 4-5, and page 4537, column 1, paragraph 1-2). Although Proudnikov et al. teach that the method can be applied to nucleic acid samples extracted from cells (see page 4541, column 2, paragraph 1), however Proudnikov et al. specifically did not teach disrupting cells to liberate nucleic acids, and use of two-buffers wherein first buffer is used to lyse the cells.

Ekenberg teaches a method for isolating genetic material wherein the method comprises (i) disrupting cells to liberate genetic material contained in the cells with guanidine isothiocyanate-containing buffer (see column 7, lines 26-40); (ii) contacting the genetic material to a column in a manner to cause the genetic material to become immobilized to the column (see column 7, lines 48-52); and eluting the genetic material from the silica column (see column 7, lines 53-65). Ekenberg also teaches more than one buffer system comprising a lysis buffer, dilution buffer, and elution buffer (see column 7, lines 26-42); the process takes less than 1 hour, and more preferably less than 20 minutes (see column 9, lines 14-23); lysis buffer contains guanidine thiocyanate (see column 17, lines 29-35) and elution buffer contains EDTA (see column 16, lines 48-65); pressure is applied to elute the genetic material from the column (see column 20, lines 14-55);the process is maintained between 30- 100 ^{0}C (see column 18 lines4-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of labeling genetic material as taught by Proudnikov

et al. with the method of isolating genetic material as taught by Ekenberg because Ekenberg states that "the genetic material obtained from this procedure can be used for analysis or further processing by molecular biological procedures and can also be used for nucleic acid probe hybridization (see page column 17, lines 1-12). Further, selection of specific temperature and buffer ratios represents routine optimization with regard to isolation of genetic material, which routine optimization parameters are explicitly recognized in Ekenberg and Proudnikov et al. As noted in *In re Aller*, 105 USPQ 233 at 235, More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the selection of specific temperature and ratios of buffer solutions performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. An ordinary practitioner would have been motivated to combine the method of the method of Proudnikov et al. with the teaching of Ekenberg because the addition of the nucleic acid isolation step using lysis buffer would reduce the process time and improve the method to rapidly isolating and labeling a nucleic acid in one procedure.

Response to Arguments:

With regard to the rejection above (Proudnikov in view of Ekenberg) Applicants' arguments have been considered and found persuasive. Applicants argue that the rejection is identical to that found in June 3, 2002 office action however the rejection is not identical because the rejection in June 3, 2002 office action is Ekenberg in view of Proudnikov et al. and not as the

above rejection. The rejection is withdrawn herein inview of the declaration submitted by Bavykin et al. on August 12, 2002.

7. With regard to the Applicants' request for the status of claims 26-27, the rejection is rewritten herein under 35 USC 103(a) as follows:

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirzabekov et al. (USPN. 5,981,734) in view of Ekenberg (USPN. 6,218,531).

Mirzabekov et al. teach a method for labeling genetic material wherein Mirzabekov et al. teach (b, and c) loading the genetic material onto a solid support to immobilize the genetic material (see column 2, lines 39-49) and fragmenting and labeling of the genetic material via creating radical-mediated process at the same time (see column 4, lines 30-67, column 5, lines 1-18); and (d) eluting the labeled genetic material from the column (see column 6, lines 37-52). Mirzabekov et al. also teach (i) contacting double-stranded nucleic acid with radical-generating complexes to produce aldehyde moieties (see column 59-67, column 5, lines 1-14); (ii) reacting the aldehyde moieties with amine to produce condensation product and contacting the condensation product with a chromophore (see column 59-67, column 5, lines 1-14, column 12, lines 35-44) (ii) the labeling of genetic material was carried at temperatures ranging from 20^0 - 37^0 C (see column 6, lines 37-66). Although Mirzabekov et al. teach that the method can be applied to nucleic acid samples extracted from cells (see column 2, lines 29-38), however Mirzabekov et al. specifically did not teach disrupting cells to liberate nucleic acids, and use of two-buffers wherein first buffer is used to lyse the cells.

Ekenberg teaches a method for isolating genetic material wherein the method comprises (i) disrupting cells to liberate genetic material contained in the cells with guanidine

isothiocyanate-containing buffer (see column 7, lines 26-40); (ii) contacting the genetic material to a column in a manner to cause the genetic material to become immobilized to the column (anerobic condition) (see column 7, lines 48-52); and eluting the genetic material from the silica column (see column 7, lines 53-65). Ekenberg also teaches more than one buffer system comprising a lysis buffer, dilution buffer, and elution buffer (see column 7, lines 26-42); the process takes less than 1 hour, and more preferably less than 20 minutes (see column 9, lines 14-23); lysis buffer contains guanidine thiocyanate (see column 17, lines 29-35) and elution buffer contains EDTA (see column 16, lines 48-65); pressure is applied to elute the genetic material from the column (see column 20, lines 14-55); the process is maintained between 30- 100 ^{0}C (see column 18 lines 4-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of labeling as taught by Mirzabekov et al with the method of isolating genetic material as taught by Ekenberg because Ekenberg states that "the genetic material obtained from this procedure can be used for analysis or further processing by molecular biological procedures and can also be used for nucleic acid probe hybridization (see page column 17, lines 1-12). Further, selection of specific temperature and buffer ratios represents routine optimization with regard to isolation of genetic material, which routine optimization parameters are explicitly recognized in Ekenberg and Mirzabekov et al. As noted in *In re Aller*, 105 USPQ 233 at 235,More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the selection of specific temperature and ratios of buffer solutions performed

was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. An ordinary practitioner would have been motivated to combine the method of the method of Mirzabekov et al. with the teaching of Ekenberg because the addition of the nucleic acid isolation step using lysis buffer would reduce the process time and improve the method to rapidly isolating and labeling a nucleic acid in one procedure.

Response to Arguments:

With reference to the rejection (Mirzabekov in view of Ekenberg et al.), Applicants' arguments have been fully considered and found not persuasive. Applicants argue that the prior art, Mirzabekov et al. does not teach a radical mediated process, and refers to Fig. 1 and 2 of the Mirzabekov patent. Applicants further argue that the instant method enables DNA and RNA production of aldehyde derivatives of nucleic acids and the production occurs via hydrogen radical excision from deoxyribose or ribose residues. Applicants arguments have been fully considered and found not persuasive. First, Applicants referring to the Fig. 1 and 2 are irrelavent to the present context, because Mirzabekov patent teaches radical mediated process in Fig. 4 and immobilization of DNA is detailed in column 11, lines 3157, column 12, lines 1- 17). Second, the argument that "production of aldehyde derivatives of nucleic acids occur via hydrogen radical excision from deoxyribose or ribose residues" is ***not*** in the claims. As stated in the MPEP 2145, "Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims". In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993), the instant claims do not recite structural limitation and specification is not be

read into the claims. Further, Mirzabekov et al teach production of aldehyde derivates of DNA (oligonucleotides) is facilitated by oxidized ribose unit (see column 11, lines 32-35).

Applicants' argue that there is no teaching or suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided by the teachings of Mirzabekov et al. in view of Ekenberg et al. An ordinary practitioner would have been motivated to combine the method of the method of Mirzabekov et al. with the teaching of Ekenberg because the addition of the nucleic acid isolation step using lysis buffer would reduce the process time and improve the method to rapidly isolating and labeling a nucleic acid in one procedure. Therefore, the rejection is maintained herein.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782 . The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 12, 2004

JEFFREY FREDMAN
PRIMARY EXAMINER